



A sterically hindered optically active pentamethine dye

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Abstract—Bis[1,3-dimethyl-3,8-(trimethylen)-indoliny]pentamethinium iodide (**5**) was synthesized by coupling *rac* 4a-methyl-2,3,4,4a-tetrahydro-1*H*-carbazole (**3**) with 1,1,3,3-tetraethoxypropane. The configuration of the dye is 2*Z*,8*E*,9*E*,10*E*,9'*E*,8'*Z* as shown by ¹H NMR spectroscopy. Starting with the enantiomerically pure carbazole (95% e.e.) the optically active pentamethine **5a** was obtained in 84% optical yield. The CD absorption of **5a** at 653 nm indicates a significant helical distortion of the chromophore. © 2001 Published by Elsevier Science Ltd.

Chiral cyanine dyes first prepared by König more than 70 years ago¹ have recently become available in sufficient structural diversity to establish a class of compounds on their own.² Their unique structural and electronic properties make them interesting for a wide range of technological applications, e.g. in non-linear optics³ and optical data storage.⁴ In the theories of optical activity they provide model chromophores to verify the predictions of chiroptical helicity rules.⁵

For steric and electronic reasons the most stable configuration of the polymethine chromophore is planar all-*E*. Bulky substituents and/or end groups may change this picture and enforce *Z*-configuration about certain bonds, which generally will induce non-planar deformations of the chromophore. If in addition chirally discriminating elements are present, CD spectroscopy can detect which way the chromophore is twisted. This is the situation found in all-*Z*-configured cyanine dyes. We have described the synthesis and chiroptical properties of optically active mono-⁵ and trimethine cyanines.⁶ For the higher homologues the required synthetic effort increases significantly. In this letter we report the synthesis of an optically active pentamethine dye in which the chromophore is forced into a partial *Z*-configuration by making the terminal double bonds part of a ring system.

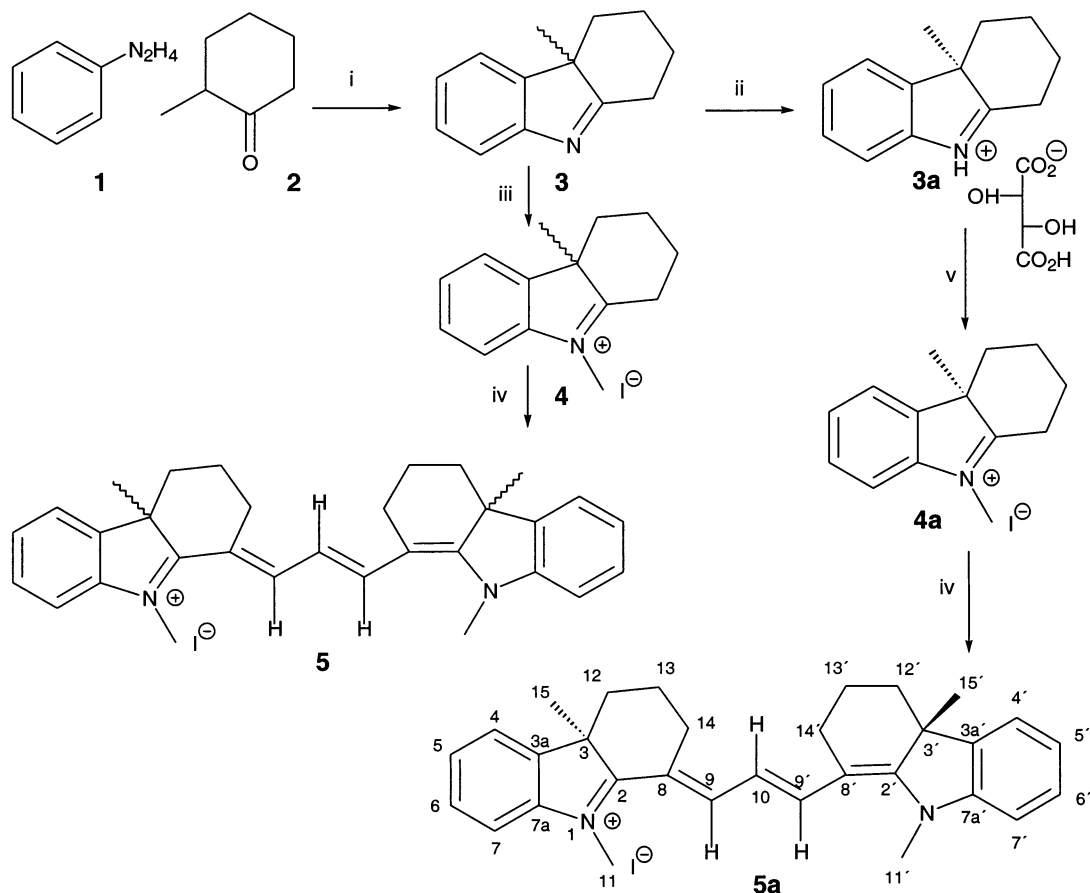
Racemic 4a-methyl-2,3,4,4a-tetrahydro-1*H*-carbazole (**3**) was prepared according to the literature⁷ by reacting phenylhydrazine (**1**) and 2-methylcyclohexanone (**2**) in the presence of glacial acetic acid (Scheme 1). Methyla-

tion with iodomethane under elevated pressure gave the iodide **4** which was coupled with 1,1,3,3-tetraethoxypropane to give in 44% yield the dark blue pentamethine **5**.

5 is expected to consist of two diastereomers, one in which the configuration at C3 and C3' is identical (the racemate) and one in which the configuration is opposite (the *meso*-form). This expectation was confirmed by ¹H NMR spectroscopy:⁸ both the singlets of the C15 and C15' and of the C11 and C11' methyl groups appear as closely spaced doublets; likewise the C10 proton and the C9 and C9' protons appear as a doublet of triplets and as a doublet of doublets, respectively. All signals can unambiguously be assigned on the basis of the enantiomerically enriched species **5a** (see below) as belonging either to the *meso* or to the racemic form of **5**. The observed difference in the signal intensities of about 3% could indicate that the formation of the *meso*-form is slightly preferred. Another indication for the diastereomeric composition of **5** comes from the ¹³C NMR spectrum in which all carbon atoms except the aromatic ones appear as doublets.

The configuration of the chromophore was determined using NMR methodology. The two central bonds of the polymethine chain are 9*E*,10*E* based on the ¹H NMR coupling constant (13.7 Hz) which corresponds to the value found in all-*E*-configured pentamethines.⁹ The configuration of the remaining bonds of the chromophore was determined by an NOE analysis of the ¹H NMR spectrum, for which two experiments were performed: (i) irradiation of the *N*-methyl protons increases the intensity of the C9 protons (and not the C10 proton); (ii) irradiation of the C10 proton increases

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Scheme 1. Synthesis of racemic **5** and optically enriched pentamethine **5a**. (i) Glacial acetic acid; (ii) D-tartaric acid; (iii) MeI; (iv) 1,1,3,3-tetraethoxypropane; (v) 0.1 M NaOH.

the intensity of the C14 protons (and not the *N*-methyl protons). With these observations the configuration of the polymethine chain can be unambiguously assigned as *2Z,8E,9E,10E,9'E,8'Z*.

To obtain optically active **5a**, the racemic carbazole **3** was resolved into its enantiomers by fractional crystallization of the salt with D-(–)-tartaric acid according to literature procedure.¹⁰ After six recrystallization steps the enantiomer excess of the sample calculated from the optical rotation at three different wavelengths had reached 95%. After removal of the anion, *N*-methylation and coupling with tetraethoxypropane, **5a** was obtained in 37% yield, mp 185°.†

In the product the amount of the *meso* form determined from the ratios of corresponding signals in the ¹H NMR spectrum was 25%. This is significantly more than the 5% which could be expected based on the optical purity of the starting carbazole. We rationalize this by assuming that under the reaction conditions racemization of the carbazole **4a** takes place, as has been described in analogous reactions (anionotropic Wagner–Meerwein rearrangement¹¹). The competition

between the condensation and racemization determines not only how much *meso*-form is produced but also the e.e. of the non-resolved racemate. For an estimate of the optical purity of **5a** we have modelled the kinetics of the system starting with a carbazole of 95% e.e. varying only the relative rates of the two competing reactions. Agreement with the experiment was found when the rate of the condensation reaction was twice the rate of the racemization reaction. This produced 25% of *meso*-form, in agreement with the NMR results, and led to an e.e. of **5a** of 84%.‡ This value was taken as the basis for the calculated $\Delta\epsilon$ values in the CD spectrum shown in Fig. 1.

Both the bathochromic shift of **5a** (Fig. 1, λ_{\max} = 653 nm in EtOH) relative to the pentamethinium dye without the trimethylene bridges (λ_{\max} = 636 nm⁹) and the reduced intensity of this band (ϵ = 55 000 l mol⁻¹ cm⁻¹) are an indication of the non-planar deformation of the chromophore which shows a negative solvatochromic effect (300 cm⁻¹ in CHCl₃). The non-planarity of the chromophore is also manifest in the CD spectrum of **5a** which shows a positive absorption ($\Delta\epsilon_{653}$ = 15) coincid-

† The IUPAC name for **5a** is (4*aR*,4*aR*)-(1*E*)-4*a*,9-dimethyl-1-[(2*E*)-3-(4*a*,9-dimethyl-3,4,4*a*,9-tetrahydro-2*H*-carbazole-1-yl)prop-2-enylidene]-2,3,4,4*a*-tetrahydro-1*H*-carbazoleium iodide.

‡ We have also run the reaction with a carbazole of lower e.e. (50%). Using the same assumptions for the kinetic model we calculate that 43% of the *meso*-form is produced (versus 40% found) and that the e.e. of the resulting pentamethine is 58%.

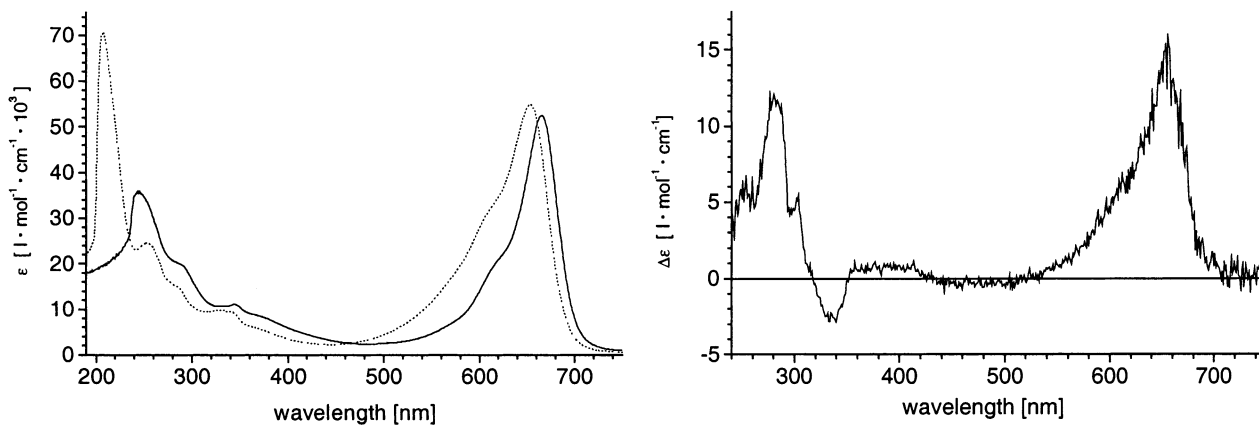


Figure 1. UV-vis spectrum of **5a** in EtOH (...) and in CHCl_3 (—) (left); $c = 1.4 \times 10^{-5}$ M. CD spectrum of **5a** in EtOH (right); $c = 4.2 \times 10^{-5}$ M.

ing with the UV-vis absorption band. In the CD spectrum the same solvatochromic behavior is observed as in the UV-vis. The magnitude of the CD is not temperature dependent: at -70°C in chloroform and -140°C in ethanol/methanol the spectra are essentially unchanged from the spectra at room temperature. This indicates that the chromophore is rigid and does not equilibrate between different conformations. According to B3LYP/6-31G** DFT geometry optimization, the chromophore is mainly twisted about the C2–C8 bond (dihedral angle 28°) and less about the neighboring C1–C2 (5°) and C8–C9 bonds (175°); the over-all helicity is *P*. Whether this structure concurs with the experimental sign of the CD band is the subject of on-going calculations.

Acknowledgements

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- ^1H NMR (CDCl_3): $\delta = 1.3$ (s, 3H, 15- CH_3), 1.31 (s, 3H, 15- CH_3), 1.8 (m, 2H, 13- CH_2), 1.9 (m, 2H, 12- CH_2), 2.1 (m, 2H, 13- CH_2), 2.2 (m, 2H, 12- CH_2), 2.7 (m, 2H, 14- CH_2), 4.1 (s, 3H, 11- CH_3), 4.11 (s, 3H, 11- CH_3), 6.3 (t, $^3J_{\text{HH}} = 13.7$ Hz, 1H, 10-CH), 6.31 (t, $^3J_{\text{HH}} = 13.7$ Hz, 1H, 10-CH), 7.1–7.3 (m, 8H, CH_{ar}), 8.2 (d, $^3J_{\text{HH}} = 13.7$ Hz, 1H, 9-CH), 8.3 (d, $^3J_{\text{HH}} = 12.7$ Hz, 1H, 9-CH); ^{13}C NMR: $\delta = 20$ (s, 13- CH_2), 26 (s, 14- CH_2), 29 (s, 15- CH_3), 29.1 (s, 15- CH_3), 32 (s, 12- CH_2), 38 (s, 11- CH_3), 38.1 (s, 11- CH_3), 49 (s, C_q , 3-C), 110 (s, C_q , 8-C), 110.5 (s, C_q , 8-C), 114.5 (s, 10-CH), 115 (s, 10-CH), 122 (s, $\text{C}_{\text{ar}}\text{-H}$), 124 (s, $\text{C}_{\text{ar}}\text{-H}$), 125 (s, $\text{C}_{\text{ar}}\text{-H}$), 129 (s, $\text{C}_{\text{ar}}\text{-H}$), 140 (s, 3a-CH), 145 (s, 7a-CH), 151 (s, 9-CH), 151.5 (s, 9-CH), 173.5 (s, 2-CH), 173.8 (s, 2-CH); MS (L-SIMS): $m/z = 435.5$.
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